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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
TELLER, ROY R	

ART UNIT	PAPER NUMBER
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/891,445	JENG ET AL.	
	Examiner	Art Unit	
	Roy Teller	1654	

-- The MAILING DATE of this communication app ars on th cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *23-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4 & 5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

This office action is in response to paper # 8, received 10/29/02. Applicant canceled claims 23-27, amended claims 1, 3-7, 10, 11, 14, 17-19 and 22. Applicant elected group I, claims 1-22 without traverse. Claims 1-22 will be examined in this office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9, 14, 18 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 recites, " is comprised of" is indefinite. Examiner suggests "comprising" be substituted for clear recitation of the claimed invention.

Claims 18 recites, "desired physiological response" and "active in an animal" are indefinite. Applicant does not define what physiological response is desired or how to determine that such a response has been achieved or give any parameters for the recited activity.

Claims 14 and 19 contains the trademark/trade name, Tween 80 . Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the

trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe and, accordingly, the identification/description is indefinite.

The use of the trademark, Tween 80, has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 18 is rejected under 35 U.S.C. 112, first paragraph, for failing to provide guidance on how to use the claimed invention.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use

the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). Additionally, the courts have determined that "... where a statement is, on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977), have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986), and are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed Cir. 1988). Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed. The instant disclosure fails to meet the enablement requirement for the following reasons:

The nature of the invention: The claimed invention is drawn to a composition of matter comprising human, equine, bovine, or porcine somatotropin (ST) and a first bioavailability enhancing constituent (BEC) comprising a non-ionic surfactant and a second BEC comprising a non-reducing carbohydrate and/or oxo-acid salt where the somatotropin and BEC are in a non-aqueous carrier.

The state of the prior art and the predictability or lack thereof in the art: Magruder (USPN

5,037,420) teaches porcine, bovine, equine, and human growth promoting hormone, somatotropin with a pharmaceutical carrier composed of the agent, a buffer comprised of sodium phosphate monobasic or sodium phosphate dibasic and a non-ionic surfactant in a non-aqueous carrier

The amount of direction or guidance present and the presence or absence of working examples: Enablement must be provided by the specification unless it is well known in the art. *In re Buchner* 18 USPQ 2d 1331 (Fed. Cir. 1991). Claim 18 recites, "desired physiological response" and "active in an animal", but do not provide any teachings in the instant specification as to how to achieve these responses (how to use the invention).

The breadth of the claims and the quantity of experimentation needed: Absent any teachings in the instant specification, the quantity of experimentation needed is considered undue.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 5, 10, 14, 15, 18, 19, and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Magruder (USPN 5,037, 420).

The claimed invention is drawn to a composition of matter comprising human, equine, bovine, or porcine somatotropin (ST) and a first bioavailability enhancing constituent (BEC) comprising a non-ionic surfactant and a second BEC comprising a non-reducing carbohydrate and/or an oxo-acid salt where the somatotropin and BEC are in a non-aqueous carrier.

Magruder teaches porcine, bovine, equine, and human growth promoting hormone, column 13, lines 66-68 and column 14, line 1. Magruder discloses somatotropin in column 14, line 11. Margurder also teaches a pharmaceutical carrier composed of the agent, a buffer and a surfactant, column 14, lines 39-40. Magruder's buffer can comprise sodium phosphate monobasic or sodium phosphate dibasic, column 15, lines 36-37. Magruder discloses nonionic surfactants such as polyoxyethylene sorbitan monooleate, polyoxyethylene stearate and Tween 80, among others, column 15, lines 58-59, 61-62, and 68. Magruder teaches a non-aqueous carrier composed of wax, column 18, line 6.

Claims 2, 3, 4, 6, 7, and 9 are included in this rejection for depending upon a rejected claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

~~Claims 1, 5, 8, 10-12, and 14-22 are rejected under 35 U.S.C. 103(a) as being~~

unpatentable over Magruder (USPN 5,037, 420) in view of Steber (USPN 5,801,141).

The claimed invention is drawn to a composition of matter comprising human, equine, bovine or porcine somatotropin (ST) and a first bioavailability enhancing constituent (BEC) comprising a non-ionic surfactant and a second BEC comprising a non-reducing carbohydrate and/or an oxo-acid salt where the somatotropin and BEC are in a non-aqueous carrier. Dependent claims recite the first BEC present from about 0.1% to about 10% by weight of the composition and the second BEC from about 1% to about 20% by weight of the composition. The first BEC comprises a non-ionic surfactant. The second BEC contains a selection of oxo-acid salts.

Magruder teaches porcine, bovine, equine, and human growth promoting hormone, column 13, lines 66-68 and column 14, line 1. Magruder discloses somatotropin in column 14, line 11. Margurder also teaches a pharmaceutical carrier composed of the agent, a buffer and a surfactant, column 14, lines 39-40. Magruder's buffer can comprise sodium phosphate monobasic or sodium phosphate dibasic from 20% to 45% , column 15, lines 36-37. Magruder discloses non-ionic surfactants such as polyoxyethylene sorbitan monooleate, polyoxyethylene stearate and Tween 80, from 0.001% to 7.5%, column 15, lines 58-59, 61-62, and 68. Magruder teaches a non-aqueous carrier composed of wax, column 18, line 6.

Magruder does not teach oxo-acid salts in the composition.

Steber teaches admixing somatotropin with a mixture of oxo-acid salts, monobasic sodium phosphate and dibasic sodium phosphate, column 15, lines 28-29 and 31-33.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have added the oxo-acid salts of Steber to the composition disclosed by Magruder , because Sterber teaches this method of elevating and maintaining elevated blood

levels of somatotropin, column 21, claim 26.

Claims 2 and 3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Magruder in view of Steber, as applied to claims 1, 14 and 18 above, and further in view of Scarborough (USPN 6,162,258).

The claimed invention is drawn to a composition of matter comprising human, equine, bovine or porcine somatotropin (ST) and a first bioavailability enhancing constituent (BEC) comprising a non-ionic surfactant and a second BEC comprising a non-reducing carbohydrate and/or an oxo-acid salt where the somatotropin and BEC are in a non-aqueous carrier. Dependent claims recite non-ionic surfactants as selected from: polyoxyethylene fatty acids esters, poloxamers, polyoxyethylene sorbitan fatty acid esters, tocopherol polyethylene glycol succinates, sugar fatty acid esters, polyoxyethylene glycerides, and polyoxyethylene vegetable oils.

Magruder in view of Steber teach a composition comprising somatotropin and a first BEC of non-ionic surfactant and a second BEC of non-reducing carbohydrates and/or oxo-acid salts as was set forth *supra.* While Magruder discloses a biological implant but does not mention the temperature of the implant, absent some evidence to the contrary, the implant would be implanted in an animal (approximately 37-39C).

Magruder in view of Steber does not teach the aforementioned non-ionic surfactants.

Scarborough teaches a polyoxyethylene sorbitan fatty acid ester and a polyoxyethylene fatty acid ester mixed with a growth hormone such as somatotropin, column 5, lines 1-2 and 5, column 6, lines 48-49.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have added the non-ionic surfactants of Scarborough to the composition disclosed by Magruder in view of Steber in order to enhance the bioavailability of somatotropin in the composition, because Scarborough teaches biocompatibility in the healing response, column 3, lines 55 and 61.

Claim 4 is rejected under 103(a) as being unpatentable over Magruder in view of Steber, as applied to claims 1, 14, and 18 above, and further in view of Mitchell (USPN 5,474,980).

The claimed invention is as described above, wherein the somatotropin is present as a zinc salt or complex.

Margruder in view of Steber teach a composition comprising somatotropin and a first BEC of non-ionic surfactant and a second BEC of non-reducing carbohydrates and/or oxo-acid salts as was set forth *supra.* Magruder in view of Steber do not teach somatotropin is present as a zinc salt or complex.

Mitchell teaches somatotropin with preferred polyvalent metals such as zinc, column 4, lines 51-52.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have admixed the zinc of Mitchell to the composition disclosed by Magruder in view of Steber, in order to enhance the bioavailability of the somatotropin in the composition, because Mitchell teaches that certain metal-associated somatotropins are useful for prolonged parenteral release of such somatotropins, see abstract.

Claims 6 and 7 are rejected under 103(a) as being unpatentable over Magruder in view of Steber, as applied to claims 1, 14 and 18 above, and further in view of Hamilton (USPN 4,816,568).

The claimed invention is as described above, wherein the second BEC is a non-reducing carbohydrate selected from one polyol and one carbohydrate ester, which include: tehalose, sucrose, mannitol, sorbitol, trehalose octaacetate, trehalose dihydrate, sucrose octaacetate, and cellobiose octaacetate.

Margruder in view of Steber teach a composition comprising somatotropin and a first BEC of non-ionic surfactant and a second BEC of non-reducing carbohydrates and/or oxo-acid salts as was set forth *supra.* Magruder in view of Steber do not teach the polyol or carbohydrate ester.

Hamilton teaches polyols selected from sucrose, mannitol, and sorbitol. The polyol can be present in amounts from about 2.5% to about 99% by weight of the total weight of the overall formulation, column 3, lines 64, 66-67, and column 4, lines 16-18.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have added the polyol stabilizer of Hamilton to the composition disclosed by Magruder in view of Steber in order to enhance the bioavailability of the somatotropin in the composition, because Hamilton teaches that growth hormones may be admixed with various stabiliziers to provide for the preservation of the soluble bioactivity of the growth hormone, see abstract.

Claims 9 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Magruder in view of Sterber, as applied to claims 1, 14, and 18 above, and further in view of Mitchell (USPN 5,739,108)

The claimed invention is drawn to a composition comprising ST and a first BEC of non-ionic surfactant and a second BEC of non-reducing carbohydrates and/or oxo-acid salts where the somatotropin and BEC are present in a non-aqueous carrier. The carrier comprises about 95% sesame oil and about 5% aluminum monostearate.

Magruder in view of Steber teaches a composition comprising somatotropin and a first BEC of non-ionic surfactant and a second BEC of non-reducing carbohydrates and/or oxo-acid salts as was set forth *supra.* Magruder in view of Steber does not teach a non aqueous carrier of about 95% sesame oil and about 5% aluminum monosterate.

Mithchell teaches a composition of somatotropin comprising a biocompatible oil, sesame oil, which constitutes a predominate part by weight of a composition , column 6, lines 27 and 35-36 together with aluminum monostearate as an antihydration agent, comprising between 1% to 10% by weight, column 7, lines 36-37 and lines 44-45. Mitchell teaches that the oil and monosterate are useful for prolonged parental release of the somatotropin (see the abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have formulated the composition disclosed by ~~Storrs~~ magruder in view of ~~Stern~~ Steber in the biocompatiable oil/ aluminum monosterate vehicles taught by Mitchell because Mitchell teaches that the oil/ monosterate vehicles are useful for prolonged parental release of somatotropin *in vivo*.

Claims 2, 3, 4, 6, 7, and 9 are included in this rejection for depending upon a rejected claim.

Conclusion

All claims are rejected

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Roy Teller whose telephone number is (703) 305-4243. The examiner can normally be reached on Monday-Friday from 5:30 am to 2:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on (703) 306-3220. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

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1654
12/2/02
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